

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
BRIAN D. GRIEDEL
170 HARBOR WAY
P.O. BOX 511
SOUTH SAN FRANCISCO, CA 94083-0511

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) **17 JUN 2005**

Applicant's or agent's file reference

EX04-017C-PC

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/23762

International filing date (day/month/year)

23 July 2004 (23.07.2004)

Priority date (day/month/year)

23 July 2003 (23.07.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/437; C07D 471/04; A61P 29/00, 35/00 and US Cl.: 514/300, 303; 546/113, 117, 118, 119, 120

Applicant

EXELIXIS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Evelyn Huang

Telephone No. (703) 308-1235

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/23762

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/23762

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☐ paid additional fees
- ☐ paid additional fees under protest
- ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
- ☒ not complied with for the following reasons:

See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1 and 23 - 25

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/23762

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-----------------------------|-----|
| Novelty (N) | Claims <u>25</u> | YES |
| | Claims <u>1, 23 and 24</u> | NO |
| Inventive step (IS) | Claims <u>25</u> | YES |
| | Claims <u>1, 23 and 24</u> | NO |
| Industrial applicability (IA) | Claims <u>1 and 23 - 25</u> | YES |
| | Claims <u>NONE</u> | NO |

2. Citations and explanations:

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by Boyd et al. The compound depicted in the abstract is encompassed by the instant claim.

Claims 1, 23 and 24 lack novelty under PCT Article 33(2) as being anticipated by Uchikawa et al. (WO 2001072749 A1). The compound depicted in the abstract, and the pharmaceutical composition, and the metabolites thereof, are encompassed by the instant claims.

Claims 1, 23 and 24 lack novelty under PCT Article 33(2) as being anticipated by Takahashi et al. (JP 06247966 A2). The compound depicted in the abstract, and the pharmaceutical composition, and the metabolites thereof, are encompassed by the instant claims.

Claims 1, 23 and 24 lack novelty under PCT Article 33(2) as being anticipated by Renhowe et al. (US 2003/0028018 A1). The compounds of Examples 46-48 (page 47), and the pharmaceutical composition, and the metabolites thereof, are encompassed by the instant claims.

Claims 1, 23 and 24 lack novelty under PCT Article 33(2) as being anticipated by JP 06199855 A2. The compounds described on pages 13 - 17, and the pharmaceutical composition, and the metabolites thereof, are encompassed by the instant claims.

Claim 25 meets the criteria set out in PCT Article 33(2) - (3), because the prior art does not teach or fairly suggest the instant method of using the inventive compound for modulating the kinase activity.

Claims 1 and 23 - 25 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry as a therapeutic agent for treating an ALK-dependent disease or condition.